Effects of Octreotide Acetate Treatment for Scleroderma Bowel

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ABSTRACT. We describe two scleroderma patients with severe gastrointestinal involvement successfully treated with octreotide acetate. The patients received daily subcutaneous infusion of octreotide acetate for three weeks. Improvement of intestinal motility was observed within two weeks after the first infusion. Remission of the patients' symptoms was maintained for more than a year after the treatment. No major side effects were observed except for slight diarrhea. Octreotide acetate could be a useful treatment not only for the early stage of scleroderma bowel but also for the advanced stage of the disease.

Key words: Octreotide acetate — pseudo obstruction — scleroderma

Scleroderma bowel is a common but life threatening manifestation in scleroderma patients. A variety of drugs, including PGF2α, dimethicone, cisapride, and antibiotics, have been administered to relieve this complication. However, symptoms are often resistant to them and the effects of these drugs, if any, last only a limited time. Once an intestinal pseudo-obstruction, the advanced manifestation of scleroderma bowel, occurs, hospitalization is often required, and it affects the prognosis of the scleroderma patient.[1)]

Octreotide acetate, which is a somatostatin analog, was developed for the treatment of acromegaly and neoplasms of the pancreas and gastrointestinal (GI) tract. It has also been administered for the treatment of insulin-dependent diabetes, gastric bleeding, and postural hypotension.[2)] Recent studies have evaluated octreotide acetate in the treatment of scleroderma bowel.[3)] In this report, we present cases of intestinal pseudo-obstruction or pneumatosis intestinalis successfully treated with octreotide acetate. The mechanism of octreotide acetate in scleroderma bowel is controversial, but our observations showed that it obviously improved the motility of the bowel in our scleroderma patients. It also provided long term remission after the treatment period, contributing to a better state of life for the involved patients.

CASE REPORTS

Case 1

A 28-year-old woman was first seen in December 1985 for Raynaud's phenomenon and digital pitting ulceration. The diagnosis of scleroderma was made clinically and histopathologically according to the criteria proposed by the Japanese Ministry of Health and Welfare. Skin sclerosis steadily

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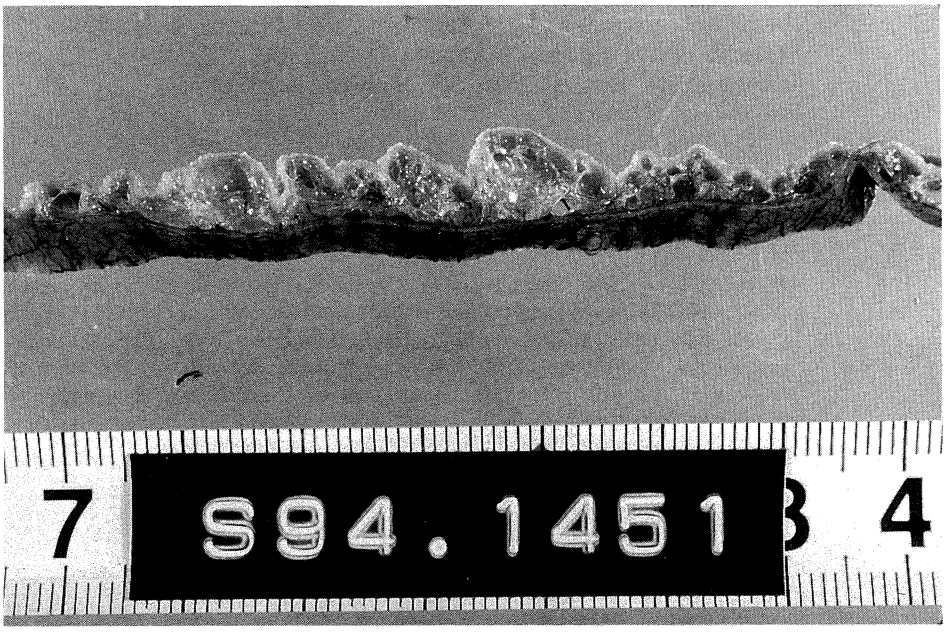

Fig 1. Pneumatosis intestinalis was observed in case 1.

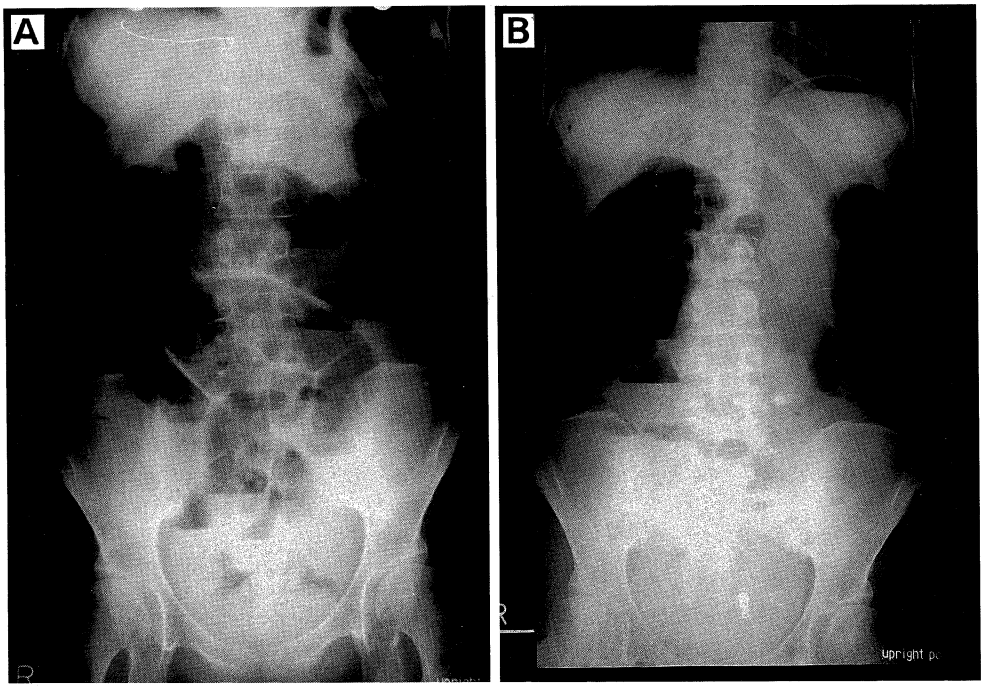

Fig 2. Case 1. A: A roentogenogram (before octreotide treatment) showing marked intestinal distension. B: Intestinal distension was dramatically improved by octreotide. A roentogenogram was taken on day 10 of treatment.

progressed, and in January 1994, she was admitted because of appetite loss, nausea, abdominal fullness and constipation. Diet therapy combined with administration of kanamycin, dimethicone and cisapride was employed but the response was poor. A month after admission, she complained of sudden severe epigastric pain and abdominal free air was observed on a plain abdominal roentgenogram. A laparotomy was performed in the Department of Surgery, Kawasaki Medical School, under a diagnosis of intestinal perforation caused by pneumatosis intestinalis (Fig 1). However, bowel symptoms remained unchanged.

Octreotide acetate treatment was applied in June 1994 according to the following protocol; octreotide acetate was subcutaneously injected daily for three weeks, 25 μg on day 1, 40 μg on day 2, 50 μg from day 3 to day 5, and 100 μg on day 6 and subsequent days. Improvement of abdominal fullness, constipation and appetite loss occurred two weeks after the first injection. Abdominal X-ray findings also remarkably improved (Fig 2A, B). She complained slight diarrhea during the treatment period, but no serious side effects were observed.

Case 2

A 47-year-old woman who had a congenital cholinesterase deficiency was first diagnosed with scleroderma in 1983. She had developed scleroderma bowel in 1986 and was treated by intermittent total parenteral nutrition in the

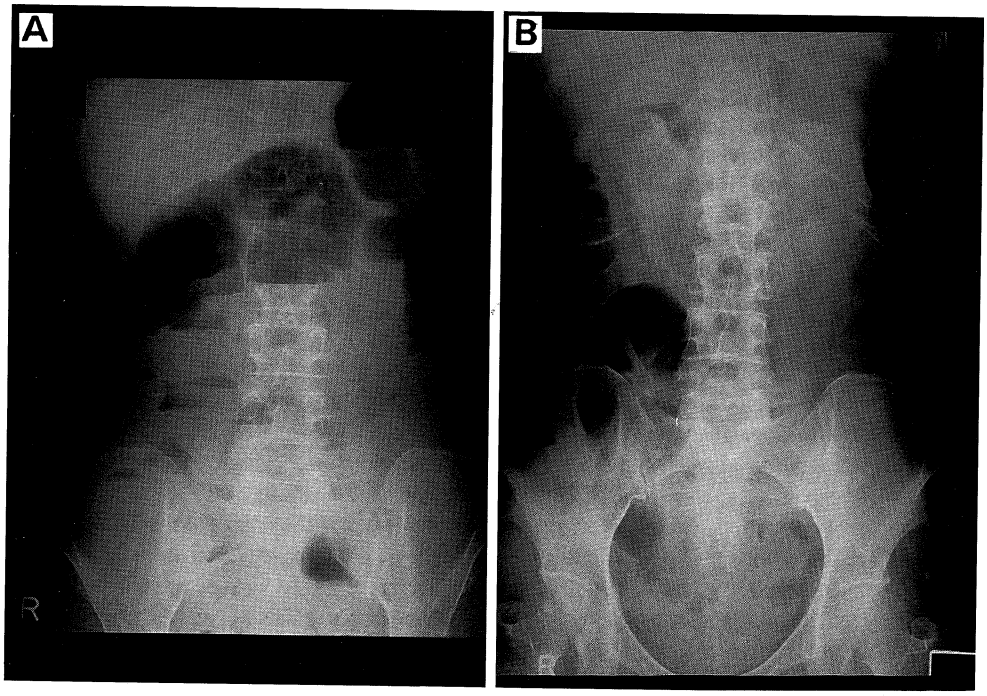

Fig 3. Case 2. A: A roentogenogram (before octreotide treatment) showing numerous air-fluid levels B: Air-fluid levels were decreased by octreotide acetate. A roentogenogram was taken on day 14 of treatment.

Department of Internal Medicine, Kawasaki Medical School. In May 1995, she was admitted because of poor nutrition caused by continuous abdominal fullness, nausea, constipation and appetite loss. An intestinal pseudo-obstruction was observed on a plain abdominal roentogenogram (Fig 3A). Neither kanamycin, cisapride, dimethicone, nor PGF2α was effective against those symptoms.

Octreotide acetate treatment was carried out in June 1995 according to the following protocol; octreotide acetate was subcutaneously injected daily for three weeks, 50 μg on the first two days, and 100 μg on the subsequent days. The bowel sounds was encouraged from a day after the first injection. Most of her bowel symptoms improved within two weeks (Fig 3B). Slight diarrhea began on day 7 of the treatment, but disappeared after the treatment period.

In the latest follow-up at our outpatient clinic in October 1996, both patients were well with regard to scleroderma bowel. During our observations, octreotide acetate did not affect other features in scleroderma such as Raynaud's phenomenon, digital autoamputation, skin sclerosis or lung fibrosis.

DISCUSSION

Small bowel hypomotility, known as *scleroderma bowel*, has been observed in 40% of scleroderma cases.[4] Scleroderma bowel basically occurs due to loss of neuromuscular GI motility in the early stage. Simultaneously systemic sclerosis involving intestinal wall, which also causes GI hypomotility, occurs. Intestinal pseudo-obstruction and bacterial overgrowth may be observed because of loss of intestinal "housekeeping" motion. In some cases, the fibrosis and bacterial overgrowth may develop into pneumatosis intestinaris, which is the most severe outcome of scleroderma bowel. Patients may have poor nutrition, bacteremia, and GI perforation late in the course of the disease. A variety of drugs have been administered for scleroderma bowel, but only a limited effect has been observed in treatments with PGF2α, dimethicone, cisapride and antibiotics.

Octreotide was first used to treat GI involvements of scleroderma by Soudah, *et al* in 1993.[3] Subsequent studies reported that octreotide acetate was effective especially in the early stage of scleroderma bowel.[5] The mechanism on the effect of octreotide in scleroderma bowel is not clear because octreotide is known to act suppressive in GI motility in normal individuals.[6] However, it is an interesting speculation that, in scleroderma bowel, the interdigestive migrating motor complex (IMC) of the GI tract is suppressed by abnormal irregular spastic waves and octreotide may encourage normal IMC by its inhibitory effect on those pathogenic waves.[3,6]

Although both patients presented in this report had advanced scleroderma bowel (case 1 had pneumatosis intestinaris and case 2 had intestinal pseudo-obstruction), their GI symptoms dramatically responded to the treatment with octreotide acetate. The effect was observed as early as two weeks after the first infusion and remission of symptoms remained long after the treatment period. No major side effects were observed. Thus, we conclude that octreotide acetate is useful for treatment not only in the early stage of scleroderma bowel but also in the advanced stage of the disease.

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